

Lars Gustafson

Psychiatric Symptoms in Presenile Dementia:
Related to Psychometric Groups and
Regional Cerebral Blood Flow

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Department of Psychiatry I, University Hospital, Lund, Sweden.

PSYCHIATRIC SYMPTOMS IN PRESENILE DEMENTIA:
RELATED TO PSYCHOMETRIC GROUPS AND
REGIONAL CEREBRAL BLOOD FLOW.

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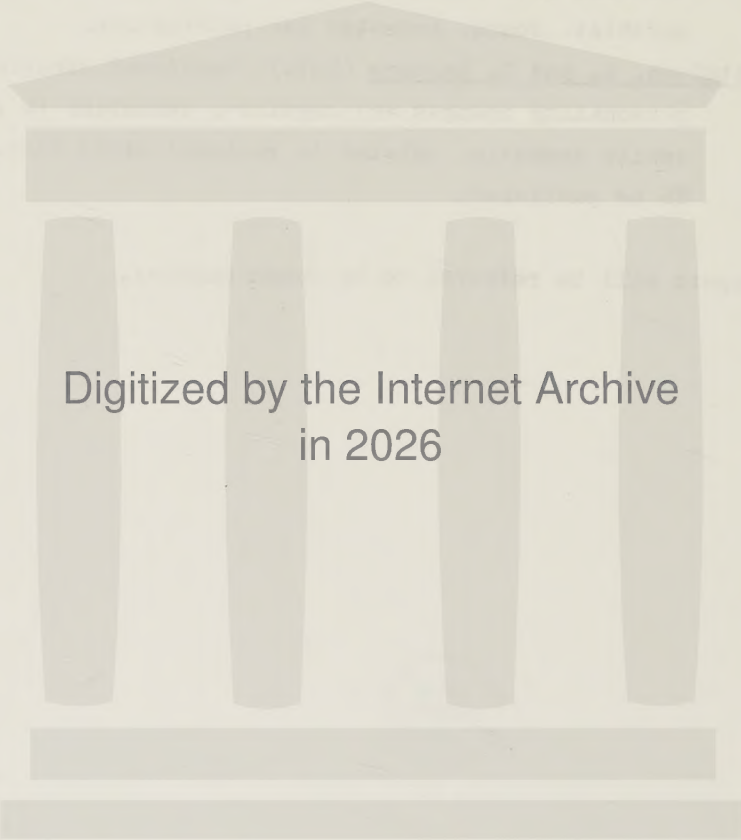


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- I. Gustafson, L. (1974): Psychiatric symptoms in dementia with onset in the presenile period. Acta psychiat. scand. Accepted for publication.
- II. Gustafson, L. and J. Risberg (1974): Regional cerebral blood flow related to psychiatric symptoms in dementia with onset in the presenile period. Acta psychiat. scand. Accepted for publication.
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INTRODUCTION.

The present thesis concerns the psychiatric symptomatology in patients with dementia starting in middle age or the pre-senium (40-65 years). During this period of life, normal aging ordinarily brings about only a small reduction of cognition and other mental functions. Presenile dementia is in the following used in a less restricted sense to designate dementia with onset in the presenile period independent of its etiology and course, and thus also includes the primary (or essential) presenile dementias, such as Alzheimer's disease, Pick's disease and Jakob-Creutzfeldt's disease.

Dementia has been defined as a "global deterioration of mental functioning in its intellectual, emotional and cognitive aspects" (Mayer-Gross, Slater and Roth 1969). The clinical, psychiatric and, especially, the psychometric description of patients with dementia, have primarily been directed upon the cognitive deterioration. The psychiatric description includes, however, to a further extent also emotional and conative disturbances and various personality reactions. The different symptoms that constitute the clinical picture of dementia are here rendered briefly in accordance with well established concepts (Mayer-Gross and Guttmann 1937, Critchley 1953, Mayer-Gross, Slater and Roth 1969): Amnesia, disturbance of attention, consciousness and orientation, lack of initiative and spontaneity, reduced stock of ideas, increased reactivity, extreme selectiveness of stimuli, affective disturbances, suspiciousness and paranoid tendencies, aphasia, agnosia and apraxia. These symptoms observed in patients with dementia may be considered either as primary, basic symptoms, which are directly related to the organic defect and/or as secondary, adaptive reactions (compensatory as well as protective) or insufficiency reactions to the effects of the organic brain disorder. Various disturbances in emotional beha-

viour have been described, such as the catastrophic reaction (Goldstein 1952, 1959), the indifference reaction (Denny-Brown, Meyer and Horenstein 1952, Critchley 1953), the various protective reactions by which the patient avoids provoking situations (Goldstein 1952), compensatory reactions (Rothschild 1942) and other active defense mechanisms against awareness of disabilities and failures (Goldstein 1959).

Investigations of the relationship between the severity of neuropathological changes in the brain and the degree of dementia, have shown inconsistent results. While some authors have questioned the correlation between pathoanatomical changes and intellectual deterioration in patients with senile dementia and arteriosclerotic psychosis (Wolf 1959, Rothschild 1937, 1942), others have found a high correlation between the cerebral changes and clinical and psychological measurements (Roth, Tomlinson and Blessed 1967, Tomlinson, Blessed and Roth 1968, 1970) or clinical groupings (Corseilis 1962).

The functional level of the brain as measured by recording of total mean cerebral oxygen consumption or blood flow has shown significant correlations with degree of mental deterioration in patients with dementia (Freyhan, Woodford and Kety 1951, Fazekas et al 1953, Lassen, Munck and Tottey 1957, Hedlund et al 1964). This relationship seems to be stronger for the dominant hemisphere than for the nondominant (Lassen, Feinberg and Lane 1960). The influence of normal aging on the cerebral blood flow has been studied. It seems as if the normal process of aging per se, at least up to the seventies, has no significant influence on brain circulation and oxygen uptake (Lassen, Munck and Tottey 1957, Dastur et al 1964).

PRESENT INVESTIGATION.

The three investigations presented here are part of a longitudinal and prospective investigation of presenile patients. The patients were followed up at regular intervals (usually one year) by means of psychiatric investigations and psychometric tests and, when possible, post mortem examinations were performed. The results from this follow-up will be presented separately.

The investigation presented here, however, deals exclusively with the patients' symptoms during a single time period at entry into the investigation. The main purposes of the investigations were:

1. to formulate psychiatric, clinical variables, which could be used for a qualitative and quantitative description of patients developing dementia.
2. to study the relationship between various types of emotional behaviour and personality changes in presenile dementia and the cognitive functional level, psychometrically defined.
3. to elucidate the relationship between symptom patterns in patients with dementia and the cerebral functional level as quantitated by the measurements of regional cerebral blood flow (rCBF).

PATIENT MATERIAL.

The present patient material consists of 57 patients (30 women and 27 men) with symptoms of dementia, the onset of which had been observed between 40 and 65 years of age (irrespective of age at first investigation). The material, which is presented in paper I, was selected to include various degrees of dementia from the incipient to the most deteriorated stage, and to be uniform in certain respects regarding preexisting psychiatric

and somatic diseases. Patients who had abused alcohol or drugs or had had chronic psychosis, endogenous intoxications or severe head injuries were excluded, as were patients with apoplexy with gross neurological symptoms. The rCBF measurements here reported on derive from 50 patients. Seven patients of the original material were excluded for technical deficiencies of the rCBF determinations (II).

FOURTEEN PSYCHIATRIC FACTORS.

All 57 patients underwent a formalized clinical evaluation by a psychiatrist using a three point rating scale of 67 symptoms. Using another similar rating scale, a nurse independently recorded her own and other staff members' observations of the patients' ward behaviour. The symptoms of the two ratings were factoranalysed and 14 clusters of symptoms (factors) were obtained from each symptom rating. The symptoms of the factors are presented in paper I, where the obtained factors are described by symptoms with the strongest factor loadings on a factor. The two factor solutions were used to evaluate the stability of the factor structures obtained and not to compare solitary symptoms of the two ratings. There was a good agreement between the structures of the two factor solutions. The main interest was focused on the factors from symptoms rated by a psychiatrist as this evaluation was considered the most standardized. When compared with clinical experience, the factors appeared to be both meaningful and easily interpretable. They showed important similarities to symptom constellations generally found in organic brain disorders.

In order to describe the patients by means of the factors in a comparable manner, a standardized score was calculated for each patient and each factor according to principles presented in paper I. These standardized factor scores were used as a quan-

titative measure of the factor symptomatology. The standardized scores do not give absolute information about the symptomatology of a patient, but rather indicate the extent to which a factor contains the symptoms of one patient compared to another, as well as compared to the total patient group. These standardized factor scores were used for calculating correlations between factors of the same or different factor solution, between factors and age characteristics (I), between factors and rCBF (II) and between factors and psychometric groups (III).

The 14 factors from symptoms rated by a psychiatrist will be presented briefly. General as well as more specific aspects of mental deterioration were presented in four factors. Amnesia-apraxia described a general, global dementia, amnesia-confusion described a more delimited aspect of bewildered outlook, memory impairment and disorientation, and agraphia-alexia had a certain similarity to the Gerstmann's syndrome. The psychomotor over-activity-euphoria factor was characterized by a loss of awareness of disabilities and of failure to regulate verbal as well as nonverbal performances. These four factors had significantly positive correlations with the patients' age at onset and age at the time of investigation. The factors depression, ixophrenia, hypochondria, paranoia and delusions were conceived of as reactions upon or attempts to compensate for various difficulties and impairments. The depression factor described by low mood and anxiety, was associated with short duration of, and a less severe stage of the dementia, while symptoms of paranoia appeared at various degrees of dementia. The ixophrenia and hypochondria factors, which bore similarity to the epileptic personality were associated with an early disease onset. Affective lability and explosive temper, which were characterized by inadequately controlled emotional expression, were related to a more advanced stage of the disease. Three factors which described various motoric dysfunctions showed no significant correlations to the

age characteristics. Unsteady gait was described by difficulties in walking, dysarthria and tremor, anarthria-mutism was described by a more or less total disinclination to speech and psychomotor retardation was described by a reduced spontaneity of mimical movements and other motoric activities.

The factor solution presented groups of symptoms, factors, which are not considered to be specific for the type of dementia here studied, but may appear in various mental diseases and organic brain disorders. The factors were considered of as reflecting a basic dimension in the material, manifested by common symptoms. These different underlying dimensions were presupposed to be related to qualitative and quantitative differences in the cerebral dysfunction. This assumption was supported by the comparison between the factors and the symptoms of different organic brain lesions (I).

PSYCHIATRIC FACTORS RELATED TO THE COGNITIVE FUNCTIONAL LEVEL.

In paper III was analysed the relationship between the psychiatric factors and different cognitive defect levels, psychometrically defined.

In a psychometric study (Hagberg and Ingvar 1974), the present patient material, as contrasted with a matched control group, could be differentiated into five groups representing successively more reduced cognition:

- C 1, no significant differences from the control group in the performance on any test.
- C 2, significant reduction only with regard to immediate memory, both verbal and spatial.
- C 3, general intellectual reduction, not including verbal functions.

C 4, general and verbal reduction with anomia, acalculia and distorted but retained spatial ability.

C 5, general reduction, aphasia, agnosia, apraxia and distorted spatial ability.

Each of these psychometric groups showed different rCBF values. A clear parallelism was found between degree of cognitive reduction and mean hemisphere flow values, especially with regard to $\bar{F}_{10}$ and $\bar{F}_g$.

The relationship between the degree of cognitive reduction, expressed in terms of the patient's membership in a psychometric group, and the patient's standardized factor scores on the 14 psychiatric factors was calculated. The psychiatric and the psychometric measurements showed a good agreement with one another in determining degree of dementia. The significant negative association between, on the one hand, the psychometric defect levels and on the other hand, the factors depression, delusions, ixophobia and hypochondria, indicate that symptoms represented by those four factors are more prominent when the cognitive reduction is less advanced. The correlations also showed that explosive temper, affective lability and psycho-motor overactivity-euphoria were more pronounced in patients with a more advanced cognitive reduction. The presence of paranoid symptoms did not show any special relationship with the level of cognitive reduction.

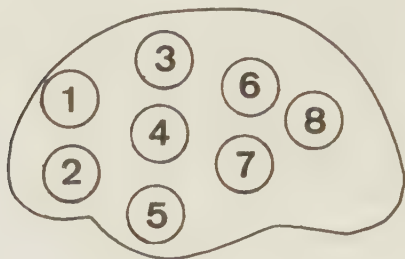
Among the 14 psychiatric factors obtained in the analysis of the patients (I), seven were selected for a combined psychiatric-psychometric description of the material (III). These factors were chosen so as to correspond with the behavioural disturbances in organic brain disorder, presented in the introduction. To compare the presence of the symptoms of these seven factors among the various psychometric groups, a mean factor score was

calculated for the patients in these groups. These mean values showed that depressive symptoms, ixophrenia and hypochondria were most common in the least cognitively deteriorated patients. Explosive temper and paranoia were more equally distributed, while affective lability and psychomotor overactivity-euphoria were prevelant among the most deteriorated patients.

The relationship between the patients' symptomatology and rCBF was investigated in 50 patients and presented in papers II and III. Preliminary analyses of these patients have been presented earlier (Ingvar and Gustafson 1970, Gustafson et al 1972 A, Gustafson et al 1972 B). rCBF was measured by means of $^{133}\text{Xenon}$ intra-arterial injection technique (Lassen et al 1963, Ingvar and Gustafson 1970, Sveinsdottir et al 1971, Lassen and Ingvar 1972). With this technique it was possible to measure and quantitate the functional level of the lateral part of one cerebral hemisphere, while subcortical and medial parts were not measured to the same extent. In the present studies, the rCBF values from eight regions of measurements were used. In Fig. 1 the average position of these regions are indicated (II). For 47 subjects measurements were made in the dominant hemisphere defined according to handedness.

In paper II the product-moment correlation between the patients' standardized factor score on 14 psychiatric factors and their rCBF values in eight cerebral regions were calculated. The factors amnesia-apraxia, amnesia-confusion and agraphia-alexia showed the highest negative correlations with flow values and relative weight of grey matter, especially in the posterior temporal and occipito-parietal regions, suggesting that the most demented patients had reduced functional level and atrophic changes in these regions. These findings are in good agreement with previous studies showing that lesions of the posterior parts of the brain produce a wide range of different intellectual and perceptual dysfunctions, as well as different types of aphasia and apraxia (Critchley 1953, Piercy and Smyth 1962, Luria 1966, 1973, Gloning, Gloning and Hoff 1968). The earlier productive symptoms of affective or other changes of personality

Fig. 1: The approximate cerebral localization of the eight regions of rCBF measurements.



Region	
frontal	{ 1. The upper frontal region
	{ 2. " lower frontal region
	{ 3. " premotor region
	{ 4. " motor region
postcentral and temporal	{ 5. " anterior temporal region
	{ 6. " parietal region
	{ 7. " posterior temporal region
	{ 8. " occipital region

were mainly found in patients with a relatively better preserved cerebral circulation. These findings fit well with the general finding that these symptoms are more frequently found in the early or less severe stages of dementia. Patients with paranoid symptoms had a high grey matter flow, especially frontally in combination with increased flow in the posterior temporal region. These results will be discussed later. The factors psychomotor overactivity-euphoria, psychomotor retardation and unsteady gait, which describe changes of psychomotor and locomotor activity, correlated with $g\%$ in the motor region.

RELATIONSHIP BETWEEN THE COMBINED PSYCHIATRIC-PSYCHOMETRIC DESCRIPTION AND REGIONAL CEREBRAL BLOOD FLOW.

In paper III, seven psychiatric symptom patterns obtained from the seven selected factors and five cognitive defect levels, psychometrically defined, formed the basis for a combined clinical description. The rCBF differences between patients having versus not-having symptoms representing the factor were analysed for each cognitive level. The symptom patterns ixophrenia, hypochondria-hysteroid traits and depression-anxiety were found mainly in less reduced patients. It was concluded that the higher cerebral function with relatively well preserved capacity for ideation and abstraction were prerequisites for these symptoms. The "compensatory" ixophrenic symptom pattern had, apart from low temporal flow, a well preserved function of the frontal area as an additional prerequisite. Hypochondria-hysteroid traits were considered a more complex, protective reaction. Patients with this symptom pattern showed fairly normal rCBF value both in mean hemisphere values and in distribution, characterized by relatively high frontal flow.

Paranoia, affective lability and explosivity-restlessness were present on all levels of dementia. Consequently, these factors

might contain components of primary lesional symptoms as well as secondary compensatory and insufficiency reactions. The paranoid symptoms were considered an adjustive reaction, which independent of the cognitive level is associated with a discrepancy of functional ability between high flow in the frontal regions and low flow in the temporo-occipital areas. The low flow of the temporo-occipital region is of special interest since this area includes important structures involved in discrimination and comprehension of sensory stimuli (Critchley 1953, Luria 1966, Gloning, Gloning and Hoff 1968). Lesions in this area may disturb analysis of incoming information and paranoia in dementia patients is tentatively interpreted as a falsely structured overcompensation for the patients' decreased comprehension of the environment. Affective lability is considered to express in the best preserved patient group, adequate but less controlled emotions. When it is found in the most deteriorated patients, it is associated with cerebral lesion shown as low functional level in the lower frontal regions involved in emotional control. Explosivity-restlessness had a typifying rCBF pattern across the different cognitive levels. It was tentatively concluded that this symptom pattern was caused by an underlying imbalance between, on the one hand emotional tension and neurophysiological prerequisites for behavioural manifestation of these emotions (high flow values in the motor areas), and on the other hand, dysfunction of the control mechanisms (low flow values in the lower frontal regions).

The psychomotor overactivity-euphoria symptom pattern found in the most deteriorated patient group, seems to be associated with the brain damage rather than an expression of secondary adjustive reaction to the lesion. These symptoms were associated with an extreme dysfunction of the most anterior parts of the frontal lobe in combination with relatively high flow postcentrally.

SUMMARY

The results summarized here show that factor analysis of psychiatric symptoms in patients with presenile dementia can be used to obtain a qualitative and quantitative description of the patients (I). The stability of the factor structure is confirmed by the similarity between the factor solutions of the two independent symptom ratings. When compared to clinical experience and symptom constellations in other types of organic brain disorder, the factors seem meaningful and easily interpretable. The validity of the factors is confirmed by their relationships with the level of cognitive reduction, psychometrically defined, and with rCBF measurements in these patients. Even if the factors are based on a rather small number of patients, they might be used to describe other types of dementia and organic brain disorder. However, in the present investigation the factors are used only for clinical description and comparison within the present patient material.

The results show that changes of emotional behaviour and personality in dementia have specific correlations with cognitive level and rCBF (II, III). In order to facilitate the understanding of the psychiatric symptom patterns, it is always necessary to consider them in relation to the degree of cognitive deficit. Certain psychiatric symptom patterns, such as ixophrenia, hypochondria-hysteroid traits and depression, are most frequent at the less reduced level of cognition and are supposed to be more influenced by the premorbid personality. These symptom patterns have positive correlations to better preserved cerebral function level as measured by the rCBF method. These three symptom patterns have, however, different rCBF pattern. Affective lability, explosivity-restlessness and paranoia are present at all levels of dementia. Consequently these factors contained components of primary lesional symptoms as well

as secondary compensatory and insufficiency reactions. This position is supported by the rCBF findings. Psychomotor over-activity-euphoria is found among the most deteriorated patients and strongly associated with dysfunction of the frontal lobes.

The results are in good agreement with previous findings on the functional organisation of the brain and the mental and behavioural disturbances following lesions of the elements of these functional systems (Goldstein 1952, 1959, Critchley 1953, Luria 1966, 1973). The results seem to support a "dynamic" interpretation of certain symptom patterns in terms of various adjustive and/or insufficiency reaction to the organic brain disorder. The present analysis found evidence for two types of relationships in presenile dementia: (1) relationships between hemisphere lesions and different behaviour syndromes within presenile dementia, and (2) relationships between remaining cerebral functions and active symptom formation within the different behaviour syndromes.

The present results deal exclusively with the patient's behaviour and cerebral functional level during one single time period, namely at his entry into the investigation. The conventional diagnosis of presenile dementias, such as Alzheimer's disease and Pick's disease are usually based, not only on observations of the patient's behaviour, but also on information about the patient's hereditarity, the clinical course of the disease and, especially, based on analysis of type, topography and severity of the cerebral lesions. The present description based on psychiatric symptom patterns, psychometrically findings and rCBF measurements will be related to the conventional diagnosis of the patients when the total material from the longitudinal part of the study will be available, including neuropathological findings post mortem.

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STUDENTLITTERATUR
LUND SWEDEN